Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	7	XUE-RU	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/06 10:54
L2	6	uromodulin NEAR promoter	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/06 11:10
L3	13	uromodulin SAME promoter	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/06 10:55
L4	23	sun NEAR tUNG-Tien	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/06 11:03
L5	11	l4 and transgenic	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/06 11:06
L6	6	l2 and transgenic	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/06 11:06
L7	11	l3 and transgenic	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/06 11:06
L8	6	(kidney ADJ specific) and uromodulin	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/06 11:07
L9	193	uromodulin	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/06 11:11
L10	8	uromodulin.clm.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/06 11:10

L11	135	l9 and transgenic	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/06 11:11
L12	10	l9 and transgenic.clm.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/06 11:11
L13	10	uromodulin and PIPLC	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/12/06 11:13
L14	119	uromodulin and (apical basal)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/06 11:13
L16	0	l13 and l14	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/12/06 11:14
L17	10	l13 and transgenic	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/12/06 11:14
L18	107	l14 and transgenic	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/12/06 11:15
L19	6	l14 and transgenic.clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/12/06 11:15
S1	11260	sun.in.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2002/04/23 16:40
S2	116	sun.in. and kidney$15	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2002/04/23 16:40
S3	11	(sun.in. and kidney$15) and urine	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2002/04/23 17:48

S4	4	(kidney ADJ specific) and (apical or basolateral)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2002/04/23 17:15
S5	10	kidney$10 ADJ specific ADJ promoter	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/03/04 15:03
S6	98	kidney ADJ specific	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2003/02/23 23:01
S7	3	(kidney ADJ specific) and uromodulin	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2003/02/23 23:01
S8	167	uromodulin	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/03/04 15:08
S9	135	uromodulin and kidney	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/03/04 14:57
S10	113	(uromodulin and kidney) AND TRANSGENIC	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/03/04 14:57
S11	7	XUE-RU	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/03/04 14:59
S12	45	sun NEAR tUNG$5	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/03/04 15:02
S13	23	sun NEAR tUNG-Tien	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/03/04 15:02

S14	104	uromodulin and (apical basal)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/03/04 15:05
S15	0	apical NEAR surface NEAR membrane NEAR targeting	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/03/04 15:07
S16	10	uromodulin and PIPLC	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/03/04 15:07
S17	1	uromodulin NEAR promoter	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/03/04 15:09
S18	5	uromodulin SAME promoter	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/03/04 15:09

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=> d his

     (FILE 'HOME' ENTERED AT 11:54:08 ON 06 DEC 2004)

     FILE 'MEDLINE, AGRICOLA, SCISEARCH, CAPLUS, MEDICONF' ENTERED AT 11:54:27
     ON 06 DEC 2004
L1          405 S UROMODULIN
L2       193149 S TRANSGENIC
L3           20 S L1 AND L2
L4           12 DUP REM L3 (8 DUPLICATES REMOVED)
L5           12 SORT L4 PY

=> d an ti so au ab pi l5 2

L5   ANSWER 2 OF 12  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2000:351690  CAPLUS
DN   133:13401
TI   Transgenic animals as bioreactors for production of protein in
     urine by kidney-specific expression using the uromodulin gene
     promoter
SO   PCT Int. Appl., 55 pp.
     CODEN: PIXXD2
IN   Wu, Xue-Ru; Sun, Tung-Tien
AB   The invention relates to recombinant DNA constructs, a method for
     producing a recombinant biol. active protein in vivo in the urine of a
     non-human mammal using a kidney-specific promoter, such as the
     uromodulin promoter, and the transgenic non-human
     mammals that serve as urine-based bioreactors for protein production  The
     recombinant DNA construct may also contain a secretion signal sequence
     operably linked to the heterologous gene.  The method for producing a
     recombinant biol. active protein in vivo in the urine of a non-human
     mammal comprises the steps of introducing the recombinant DNA construct
     into a fertilized embryo to produce a transgenic non-human
     mammals expressing and secreting the protein in the urine, and collecting
     the urine to recover the protein.  The uromodulin promoter is
     preferably of mouse, cattle, or rat, and the transgenic
     non-human mammal is goat, cow, sheep, pig, or horse.  The nucleotide
     sequences of the mouse and goat uromodulin gene promoter region
     were obtained.  Recombinant production of human growth hormone in the urine of
     transgenic mouse using the uromodulin promoter is
     described. (no data).
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     --------------      ----   --------    -------------------    --------
PI   WO 2000029608        A1    20000525    WO 1999-US26870        19991112
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
             CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
             IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
             MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
             SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     EP 1135518          A1    20010926    EP 1999-958952         19991112
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO


=>
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FILE 'MEDLINE, AGRICOLA, SCISEARCH, CAPLUS, MEDICONF' ENTERED AT 11:54:27 ON 06 DEC 2004

L1 405 S UROMODULIN
L2 193149 S TRANSGENIC
L3 20 S L1 AND L2
L4 12 DUP REM L3 (8 DUPLICATES REMOVED)
L5 12 SORT L4 PY

=> d an ti so au ab pi l5 1-12

L5 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:375662 CAPLUS
DN 131:28628
TI Methods for the degradation and detoxification of organic material using urine produced by **transgenic** animals
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
IN Lubon, Henryk; Paleyanda, Rekha; Drohan, William; Velander, William
AB This invention applies technol. advancements in the field of **transgenics** to manage animal, plant, industrial, and agricultural related wastes that are potential environmental pollutants. This method involves producing a non-human **transgenic** animal that produces a protein in its urine that degrades or detoxifies organic material, and has stably integrated into its genome an exogenous gene encoding a protein that is detectable in the urine. Thus, a DNA construct used in producing the **transgenic** animal, a **transgenic** animal that produces such protein in its urine, and a method of degrading or detoxifying organic materials also is provided. Also, a facility comprising the **transgenic** animal and a structure containing such animal is described.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9928463	A2	19990610	WO 1998-US25193	19981201
WO 9928463	A3	19990910		
W: AU, CA, JP, MX				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 2002184655	A1	20021205	US 1997-982284	19971201
AU 9916064	A1	19990616	AU 1999-16064	19981201
EP 1036176	A2	20000920	EP 1998-960480	19981201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001525171	T2	20011211	JP 2000-523339	19981201

L5 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:351690 CAPLUS
DN 133:13401
TI **Transgenic** animals as bioreactors for production of protein in urine by kidney-specific expression using the **uromodulin** gene promoter
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
IN Wu, Xue-Ru; Sun, Tung-Tien
AB The invention relates to recombinant DNA constructs, a method for producing a recombinant biol. active protein in vivo in the urine of a non-human mammal using a kidney-specific promoter, such as the **uromodulin** promoter, and the **transgenic** non-human mammals that serve as urine-based bioreactors for protein production The recombinant DNA construct may also contain a secretion signal sequence operably linked to the heterologous gene. The method for producing a recombinant biol. active protein in vivo in the urine of a non-human mammal comprises the steps of introducing the recombinant DNA construct into a fertilized embryo to produce a **transgenic** non-human mammals expressing and secreting the protein in the urine, and collecting the urine to recover the protein. The **uromodulin** promoter is preferably of mouse, cattle, or rat, and the **transgenic** non-human mammal is goat, cow, sheep, pig, or horse. The nucleotide sequences of the mouse and goat **uromodulin** gene promoter region

were obtained. Recombinant production of human growth hormone in the urine of **transgenic** mouse using the **uromodulin** promoter is described. (no data).

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000029608	A1	20000525	WO 1999-US26870	19991112
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1135518	A1	20010926	EP 1999-958952	19991112
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

L5 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:191195 CAPLUS
DN 132:247143
TI Expression of recombinant proteins in the urine of **transgenic** animals
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
IN Karatzas, Costas N.
AB The invention provides methods which generate a recombinant polypeptide that is secreted into the urine of a **transgenic** animal. The expression of the provided polypeptide is driven by the **uromodulin** gene promoter or other promoters from genes whose products are specifically expressed in the kidney. The generation of recombinant proteins utilizing an animal as a bioreactor has the advantage of producing a recombinant protein that is likely properly folded.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000015772	A2	20000323	WO 1999-IB1609	19990916
	WO 2000015772	A3	20000720		
	W: AU, BR, CA, HU, JP, NZ				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2343104	AA	20000323	CA 1999-2343104	19990916
	AU 9957553	A1	20000403	AU 1999-57553	19990916
	EP 1112353	A2	20010704	EP 1999-944741	19990916
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002525047	T2	20020813	JP 2000-570299	19990916

L5 ANSWER 4 OF 12 MEDLINE on STN
AN 2002452258 MEDLINE
TI The use of the **uromodulin** promoter to target production of recombinant proteins into urine of **transgenic** animals.
SO Transgenic research, (2002 Aug) 11 (4) 425-35.
Journal code: 9209120. ISSN: 0962-8819.
AU Zbikowska Halina M; Soukhareva Nadia; Behnam Reza; Chang Rosemary; Drews Roman; Lubon Henryk; Hammond David; Soukharev Serguei
AB A **uromodulin** promoter has been isolated, sequenced, and used to generate two sets of **transgenic** mice for expression of the lacZ marker gene and for production of the human recombinant erythropoietin (rhEPO) in urine. We demonstrated that the 5.6-kb fragment of the **uromodulin** gene containing the 3.7-kb promoter area and, both the first exon and part of the second exon, were sufficient to provide kidney-specific expression of the lacZ gene. Histological analysis of the lacZ expression pattern revealed beta-galactosidase activity specifically in the thick limb of Henle's loop. However, due to random integration of the transgene, ectopic expression was detected in some **transgenic** lines. Analysis of the EPO-**transgenic** mice showed that rhEPO was secreted into the urine of founder mice (up to 6 ng/ml). We were able to breed and analyze only two sublines with a very low expression level of

rhEPO (up to 260 pg/ml). All of our **transgenic** mice expressing rhEPO in urine developed disease symptoms similar to polycythemia in humans. These included a considerable increase in red blood cell counts, hemoglobin concentration, and hematocrit concomitant with severe thrombocytopenia, all of which were detected in the rhEPO-expressing mice. Although our model did not prove to be beneficial for commercial production of rhEPO, we concluded that the **uromodulin** promoter could be useful for expression of other important therapeutic proteins into the urine of **transgenic** animals.

L5 ANSWER 5 OF 12 MEDLINE on STN
AN 2002361590 MEDLINE
TI **Uromodulin** promoter directs high-level expression of biologically active human alpha1-antitrypsin into mouse urine.
SO Biochemical journal, (2002 Jul 1) 365 (Pt 1) 7-11.
Journal code: 2984726R. ISSN: 0264-6021.
AU Zbikowska Halina M; Soukhareva Nadia; Behnam Reza; Lubon Henryk; Hammond David; Soukharev Serguei
AB We have recently shown that the regulatory sequence of the **uromodulin** gene, containing the 3.7 kb promoter, exon 1 and a part of exon 2, provided for kidney-specific expression of the reporter lacZ gene in **transgenic** mice [Zbikowska, Soukhareva, Behnam, Chang, Drews, Lubon, Hammond and Soukharev (2002) **Transgenic** Res., in the press]. In the present study, we generated **transgenic** mice harbouring the regulatory sequence of the **uromodulin** gene to direct the expression of human alpha1-antitrypsin (alpha1AT) into urine. Of the 13 founder mice that tested positive by PCR, seven showed the presence of the human protein in their urine. The concentration of the recombinant human (rh) alpha1AT in the urine, estimated by using ELISA, ranged from 0.5 to 14 microg/ml in the F(0)-generation mice, and reached up to 65 microg/ml in the F1 generation. The transgenically produced rh alpha1AT was found to be N-glycosylated and biologically active. The N-terminal sequence analysis confirmed the identity of the human protein and revealed that the recombinant alpha1AT was correctly processed with the signal peptide cleaved off. Our results demonstrate for the first time that the **uromodulin** regulatory sequence provides a very attractive option for the potential large-scale production of functional therapeutic proteins in livestock.

L5 ANSWER 6 OF 12 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2002:214428 SCISEARCH
TI Isolation of mouse THP gene promoter and demonstration of its kidney-specific activity in **transgenic** mice
SO AMERICAN JOURNAL OF PHYSIOLOGY-RENAL PHYSIOLOGY, (APR 2002) Vol. 282, No. 4, pp. F608-F617.
Publisher: AMER PHYSIOLOGICAL SOC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA.
ISSN: 0363-6127.
AU Zhu X H; Cheng J; Gao J; Lepor H; Zhang Z T; Pak J; Wu X R (Reprint)
AB Tamm-Horsfall protein (THP), the most abundant urinary protein synthesized by the kidney epithelial cells, is believed to play important and diverse roles in the urinary system, including renal water balance, immunosuppression, urinary stone formation, and inhibition of bacterial adhesion. In the present study, we describe the isolation of a 9.3-kb, 5'-region of the mouse THP gene and show the highly conserved nature of its proximal 589-bp, 5'-flanking sequence with that in rats, cattle, and humans. We also demonstrate using the **transgenic** mouse approach that a 3.0-kb, proximal 5'-flanking sequence is sufficient to drive the kidney-specific expression of a heterologous reporter gene. Within the kidney, transgene expression was confined to the renal tubules that endogenously expressed the THP protein, which suggests specific transgene activity in the thick ascending limb of the loop of Henle and early distal convoluted tubules. Our results establish the kidney- and nephron-segment-specific expression of the mouse THP gene. The availability of the mouse THP gene promoter that functions in vivo should facilitate additional studies of the molecular mechanisms of kidney-specific gene regulation and should provide new molecular tools for better understanding renal physiology and disease through nephron-specific gene

targeting.

L5 ANSWER 7 OF 12 MEDLINE on STN
AN 2003218484 MEDLINE
TI Kidney-specific activity of the bovine **uromodulin** promoter.
SO Transgenic research, (2003 Apr) 12 (2) 191-201.
Journal code: 9209120. ISSN: 0962-8819.
AU Kim Hun-Taek; Song In-Young; Piedrahita Jorge
AB A 10-kilobase (kb) lambda bacteriophage bovine genomic clone containing 5.4 kb of the 5'-flanking region, exons, and introns of bovine **uromodulin** gene was isolated. **Transgenic** mice containing 3.9 kb of the bovine **uromodulin** promoter and a lacZ reporter gene were generated by pronuclear microinjection. RT-PCR and northern blot analyses of transgene expression in various tissues of founder and F1 mice showed that the transgene was expressed exclusively in the kidney. In situ hybridization and histochemistry for lacZ demonstrated that transgene expression was restricted to tubule epithelial cells of the loop of Henle in the kidney. Stepwise 5' deletion analysis revealed that transfection of luciferase reporter constructs fused to various proximal 5'-flanking regions of the bovine **uromodulin** gene markedly increased luciferase activity in mouse renal epithelial cells but not in mesenchymal cells and that the most critical cis elements of the **uromodulin** gene are located within the 600 bp upstream region.

L5 ANSWER 8 OF 12 MEDLINE on STN
AN 2003218480 MEDLINE
TI Renal tubule-specific expression and urinary secretion of human growth hormone: a kidney-based **transgenic** bioreactor growth.
SO Transgenic research, (2003 Apr) 12 (2) 155-62.
Journal code: 9209120. ISSN: 0962-8819.
AU Zhu Xinhua; Cheng Jin; Huang Liwei; Gao Jin; Zhang Zhong-Ting; Pak Joanne; Wu Xue-Ru
AB Tissue-specific expression of human genes and secretion of human proteins into the body fluids in **transgenic** animals provides an important means of manufacturing large-quantity and high-quality pharmaceuticals. The present study demonstrates using **transgenic** mice that a 3.0 kb promoter of the mouse Tamm-Horsfall protein (THP, or **uromodulin**) gene directs the specific expression of human growth hormone (hGH) gene in the kidney followed by the secretion of hGH protein into the urine. hGH expression was detected in renal tubules that actively produce the THP, that is, the ascending limb of Henle's loop and distal convoluted tubules. Up to 500 ng/ml of hGH was detected in the urine, and this level remained constant throughout the 10-month observation period. hGH was also detectable in the stomach epithelium and serum in two of the **transgenic** lines, suggesting position-dependent effects of the transgene and leakage of hGH from the site of synthesis into the bloodstream, respectively. These results indicate that the 3.0 kb mouse THP promoter is primarily kidney-specific and can be used to convert kidney into a bioreactor in **transgenic** animals to produce recombinant proteins. Given the capacity of urine production independent of age, sex and lactation, the ease of urinary protein purification, and the potentially distinct machinery for post-translational modifications in the kidney epithelial cells, the kidney-based **transgenic** bioreactor may offer unique opportunities for producing certain complex pharmaceuticals.

L5 ANSWER 9 OF 12 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2003:972317 SCISEARCH
TI Untraditional methods for targeting the kidney in **transgenic** mice
SO AMERICAN JOURNAL OF PHYSIOLOGY-RENAL PHYSIOLOGY, (DEC 2003) Vol. 285, No. 6, pp. F1027-F1033.
Publisher: AMER PHYSIOLOGICAL SOC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA.
ISSN: 0363-6127.
AU Bianco R A; Keen H L; Lavoie J L; Sigmund C D (Reprint)
AB With the completion of the human genome project and the sequencing of

many genomes of experimental models, there is a pressing need to determine the physiological relevance of newly identified genes. Gene-targeting approaches have become an important tool in our arsenal to dissect the significance of genes expressed in many tissues. A wealth of experimental models has been made to assess the role of gene expression in renal function and development. The development of new and informative models is presently limited by the anatomic complexity of the kidney and the lack of cell-specific promoters to target the numerous diverse cell types in that organ. Because of this, new approaches may have to be developed. In this review, we will discuss several untraditional methods to target gene expression to the kidney. These approaches should provide some additional tricks and tools to help in developing additional informative models for studying renal physiology.

L5 ANSWER 10 OF 12 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2003:814761 SCISEARCH
TI Making recombinant proteins in animals - different systems, different applications
SO TRENDS IN BIOTECHNOLOGY, (SEP 2003) Vol. 21, No. 9, pp. 394-399.
Publisher: ELSEVIER SCIENCE LONDON, 84 THEOBALDS RD, LONDON WC1X 8RR, ENGLAND.
ISSN: 0167-7799.
AU Dyck M K; Lacroix D; Pothier F; Sirard M A (Reprint)
AB **Transgenic** animal bioreactors represent a powerful tool to address the growing need for therapeutic recombinant proteins. The ability of **transgenic** animals to produce complex, biologically active recombinant proteins in an efficient and economic manner has stimulated a great deal of interest in this area. As a result, genetically modified animals of several species, expressing foreign proteins in various tissues, are currently being developed. However, the generation of **transgenic** animals is a cumbersome process and remains problematic in the application of this technology. The advantages and disadvantages of different **transgenic** systems in relation to other bioreactor systems are discussed.

L5 ANSWER 11 OF 12 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2003:498638 SCISEARCH
TI Thick ascending limb-specific expression of Cre recombinase
SO AMERICAN JOURNAL OF PHYSIOLOGY-RENAL PHYSIOLOGY, (JUL 2003) Vol. 285, No. 1, pp. F33-F39.
Publisher: AMER PHYSIOLOGICAL SOC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA.
ISSN: 0363-6127.
AU Stricklett P K; Taylor D; Nelson R D; Kohan D E (Reprint)
AB Evaluation of thick ascending limb (TAL) function has been hindered by the limited ability to selectively examine the function of this nephron segment in vivo. To address this, a Cre/loxP strategy was employed whereby the Tamm-Horsfall (THP) promoter was used to drive Cre recombinase expression in **transgenic** mice. The THP gene was cloned from a mouse genomic library, and 3.7 kb of the mouse THP 5'-flanking region containing the first noncoding exon of the THP gene were inserted upstream of an epitope-tagged Cre recombinase (THP-CreTag). THP-CreTag **transgenic** mice were bred with ROSA26-enhanced yellow fluorescent protein (eYFP) mice (contain a loxP-flanked "STOP" sequence 5' to eYFP), and doubly heterozygous offspring were analyzed. THP and eYFP were expressed in an identical pattern with predominant localization to the renal outer medulla without expression in nonrenal tissues. eYFP did not colocalize with thiazide-sensitive cotransporter (distal tubule) or neuronal nitric oxide synthase (macula densa) expression. THP mRNA expression was detected only in kidney, whereas CreTag mRNA was also present in testes. These data indicate that THP-CreTag **transgenic** mice can be used for TAL-specific gene recombination in the kidney.

L5 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:344178 CAPLUS
DN 140:405503
TI The kidney and the bladder of **transgenic** animals as bioreactors?

SO Biotechnologia (2004), (1), 20-31
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AU Zbikowska, Halina Malgorzata
AB A review. Mammary gland-specific expression of human genes and secretion of human proteins into the milk of **transgenic** farm animals provides an important tool for manufacturing of many valuable pharmaceuticals. More recently, attention has focused on urine-based expression systems as a much more cost-effective technol. Successful application of this technol., however, requires the definition of several crucial regulatory elements that direct production of the protein into the urinary tract. To date, the 5' flanking region of either the uroplakin 11 (UPII) or **uromodulin** (THP) genes were used to drive the expression of heterologous proteins in the bladder or kidney epithelium of the **transgenic** mice, resp. Herein, the progress and current limitations in this field are presented. Other currently known urine-specific protein genes are also described.